Received:
22 January 2014

Revised:
30 April 2014

Accepted:
12 May 2014

doi: 10.1259/bjr.20140079

Cite this article as:

Thieme SF, Meinel FG, Graef A, Helck AD, Reiser MF, Johnson TRC. Dual-energy CT pulmonary angiography in patients with suspected pulmonary embolism: value for the detection and quantification of pulmonary venous congestion. *Br J Radiol* 2014;87:20140079.

FULL PAPER

Dual-energy CT pulmonary angiography in patients with suspected pulmonary embolism: value for the detection and quantification of pulmonary venous congestion

S F THIEME, F G MEINEL, A GRAEF, A D HELCK, M F REISER and T RC JOHNSON

Institute for Clinical Radiology, Ludwig-Maximilians-University Hospital Munich, Munich, Germany

Address correspondence to: Dr Sven Thieme
E-mail: sven.thieme@med.uni-muenchen.de

Objective: To evaluate if vascular and pulmonary parenchymal enhancement values in dual-energy (DE) CT pulmonary angiography (CTPA) can suggest the diagnosis of pulmonary congestion.

Methods: DE-CTPA images of 90 out of 1321 patients negative for pulmonary embolism showed signs of congestive heart failure. We measured DE-derived pulmonary parenchymal [perfused blood volume (PBV)], pulmonary artery (PA) and left atrium (LA) enhancement values in these patients and in 142 control patients. Enhancement values were compared between the populations and correlated with serum values of B-type natriuretic peptide (BNP) and proBNP, where available.

Results: No significant difference of PBV but significant differences of mean PA and LA enhancement and individual enhancement differences (PA – LA) were found between the populations. PA – LA was higher

in patients with elevated BNP and proBNP and was positively correlated with these values. Receiver operating characteristic analysis revealed a moderate discriminatory power of the PA – LA difference for the presence of cardiac biomarker elevations.

Conclusion: PBV in DE-CTPA is not altered in patients with signs of congestive heart failure. However, differences in enhancement values in the pre- and post-pulmonary vessels were found in comparison with the control population.

Advances in knowledge: Altered pulmonary vascular haemodynamics in pulmonary venous congestion are not reflected in dual-energy-derived PBV maps. In the diagnosis of left heart failure in patients with chest pain and dyspnoea, density measurements in the pulmonary artery and in the left atrium in CTPA images may be a helpful diagnostic tool.

In the diagnostic algorithms for patients with acute dyspnoea, CT pulmonary angiography (CTPA) plays a major role, specifically in cases when pulmonary embolism (PE) is suspected. Whenever no PE can be detected, radiologists face the challenge to detect alternative pathological thoracic findings. An undiagnosed acute or chronic left heart failure with pulmonary congestion can be an alternative cause of acute dyspnoea. Although there are some direct and indirect CT criteria that suggest the diagnosis of congestive heart failure with pulmonary venous hypertension (e.g. dilated pulmonary veins with a blurry appearance of the vessel walls, thickening of the interlobular septal lines, ground-glass opacities/alveolar oedema, pleural effusions and an enlargement of the left atrium and/or ventricle), the diagnosis of left heart failure on the basis of CT findings is often equivocal and rather rater dependent. For suspected left heart failure, chest radiography represents the primary diagnostic tool rather than CT. Still, if CTPA is performed in chest pain workup, an improved, more

objective diagnosis of congestive heart failure would be desirable.

Dual-energy CTPA (DE-CTPA) can quantify the iodine-related pulmonary beam absorption and thus allow an automated, reader-independent, software-based quantification of the pulmonary content of iodinated contrast material [termed “perfused blood volume” (PBV)].¹ Based on the assumption that an impaired left heart function leads to variances in the pulmonary blood content and in the dynamics of the pulmonary passage of the contrast bolus, we tried to find out if measured absorption values in iodine-enhanced DE-CTPA, that is, DE-based pulmonary PBV values as well as density measurements in the pulmonary trunk and the left atrium, can be helpful in the diagnosis of pulmonary congestion.

For this purpose, we retrospectively compared pulmonary parenchymal, pulmonary artery (PA) and left atrium (LA) enhancement values in patients with CT signs of pulmonary

congestion with those from patients with no detectable cardiopulmonary pathologies in DE-CTPA and correlated those values with serum levels of established left heart insufficiency markers [cardiac peptides: B-type natriuretic peptide (BNP) and proBNP].

METHODS AND MATERIALS

Ethical approval

The responsible ethics committee waived ethical approval and individual informed consent for this retrospective analysis. All patients provided written informed consent to the clinically indicated CTPA examination.

CT image acquisition

All DE-CTPAs were performed on a dual-source CT system (Somatom® Definition Flash; Siemens Healthcare, Forchheim, Germany). 85 ml of contrast material (Iopromide, Ultravist® 370; Bayer Schering Pharma, Berlin, Germany) were administered via an antecubital vein at a flow rate of 5 ml s^{-1} , followed by 50 ml of saline, injected at the same flow rate. Examinations were started using a bolus-tracking technique with a threshold of 100 HU in the pulmonary trunk and an additional delay of 7 s. A caudocranial direction was chosen. A combination of a tin-filtered (Sn) 140-kVp spectrum and a 100-kVp spectrum was used. Collimation was set to $32 \times 0.6 \text{ mm}$. Pitch was 0.5 at a rotation time of 0.28 s. Mean CT dose index (CTDI) and dose length product (DLP) were 9.6 ± 2.3 and $302 \pm 79 \text{ mGy} \times \text{cm}$, respectively, corresponding to an effective radiation dose of 4.2 mSv (using a standard conversion factor for chest CT of $0.0161 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$).²

CT image reconstruction

An axial orientation was chosen. For the reconstruction of CTPA images, a specific DE medium soft convolution kernel (D30) was used. Slice thickness was 1.5 mm with an increment of 1.0 mm. Average images from both DE data sets, similar to standard 120 kVp reconstructions, were generated.

CT density measurements and quantification of pulmonary perfused blood volume

Lung PBV was automatically quantified using the respective Syngo® DE software v. VE32B application (DE lung PBV; Siemens Healthcare, Erlangen, Germany). This analysis quantifies lung PBV by measuring the pulmonary parenchymal enhancement in relation to the contrast enhancement in a reference vessel.³ The pulmonary trunk was defined as a reference vessel, and a standardized 0.5-cm^2 region of interest (ROI) was placed within the pulmonary trunk. Lung PBV was automatically calculated as (mean pulmonary parenchymal enhancement in HU/mean enhancement in the pulmonary trunk in HU)/calibration factor 0.15 (Figure 1).

In order to correctly quantify pulmonary enhancement in patients with severe congestion/oedema with increased lung density due to ground-glass opacities, the upper threshold for the algorithm was adapted in patients with ground-glass opacities and set to -300 HU .

Another 0.5-cm^2 ROI was placed in the left atrium for an additional density measurement.

All measured enhancement values in the pulmonary trunk and the left atrium were recorded.

Image quality control

All examinations with severe artefacts, inadequate enhancement of the pulmonary vasculature and/or inadequate timing were excluded. For this purpose, density values in the pulmonary trunk were measured, and artefacts in the PBV maps (from cardiac motion, breathing or concentrated contrast material) were visually assessed. All studies with severe artefacts were excluded. Since lung PBV values may become unreliable with insufficient enhancement of the pulmonary trunk, all examinations with an enhancement of the pulmonary trunk of $<150 \text{ HU}$ were excluded.

Figure 1. Axial cross-sectional images of a 74-year-old male patient with signs of pulmonary congestion. Lung window shows dilated pulmonary veins and bronchial cuffing as well as thickened septal lines and bilateral pleural effusion (a). Lung perfused blood volume image (b) visualizes colour-coded iodine mapping in the pulmonary parenchyma.

Patient selection

We defined two patient groups on the basis of the following criteria:

- Inclusion criteria for patient Group #1 (congestion group):
 - (1) clinically indicated DE-CTPA negative for PE
 - (2) morphologic signs of pulmonary venous congestion present in CT.
- Exclusion criteria for patient Group #1 (congestion group):
 - (1) DE-CTPA with severe artefacts or inadequate pulmonary vascular enhancement
 - (2) any thoracic pathologies other than left heart failure and/or pulmonary congestion known or detected on DE-CTPA.
- Inclusion criteria for patient Group #2 (control group):
 - (1) clinically indicated DE-CTPA negative for PE
 - (2) no signs of pulmonary venous congestion present.
- Exclusion criteria for patient Group #2 (control group):
 - (1) DE-CTPA with severe artefacts or inadequate vascular enhancement below 150 HU
 - (2) any thoracic pathologies, either known or detected on DE-CTPA.

Between May 2009 and November 2011, 1321 DE-CTPAs for suspected PE were performed at our institution, 1097 of whom were negative for acute PE. The respective 1097 radiology reports (including clinical history and indication) were reviewed for any thoracic pathologies (either known or newly detected). 727 examinations were excluded because of thoracic pathologies other than pulmonary venous congestion.

Signs of pulmonary venous congestion (*i.e.* dilated pulmonary veins or vascular blurring with or without thickened septal lines, ground-glass opacities, pleural effusions or left ventricular enlargement) were described and rated as pulmonary congestion in the reports of 114 patients. In 12 of these patients, no DE data sets had been archived. Three patients were excluded owing to inadequate vascular enhancement (defined as enhancement of <150 HU in the pulmonary trunk). Nine patients were excluded from the analysis owing to severe artefacts (predominantly streak artefacts from dense contrast material in the superior cava vein) or inflammatory consolidations or atelectasis. The remaining 90 patients were included and defined as congestion group (Group #1).

The most frequent other pathologies described in the CT reports included pleural effusion without signs of congestion ($n = 246$), atelectasis ($n = 227$), pneumonia ($n = 223$), chronic obstructive pulmonary disease (COPD)/pulmonary emphysema ($n = 173$), signs of PA hypertension ($n = 137$), malignancy with pulmonary involvement ($n = 115$) and interstitial lung disease ($n = 81$). Of 37 of the remaining 256 examinations, no DE data sets had been archived. Severe artefacts were found in 56 data sets and inadequate enhancement <150 HU in the pulmonary trunk in 21 examinations. The remaining 142 patients could be included in the data analysis as control group (Group #2).

The large cohort of 1097 patients without PE as well as our control group have been published before in a previous study performed at our institution, establishing ranges of normal for DE lung PBV that can be used in further studies.¹ However, our

patient Group #1 represents a different subpopulation that has not been published before.

CT data analysis

Visual assessment

The reconstructed CTPA images were reviewed in consensus by a board-certified radiologist (TRCJ) and a radiology resident (SFT) with more than 10 and 6 years' experience in thoracic imaging, respectively. The diagnoses of either no detectable cardiopulmonary morbidity in the control group or signs of pulmonary venous congestion and no other cardiopulmonary pathological findings in the congestion group were confirmed. The diagnoses of the radiology reports could be confirmed in all cases in both groups.

Pulmonary venous congestion was presumed when the presence of dilated pulmonary veins and/or blurring of the pulmonary venous vessel walls were confirmed. Additional findings (thickened septal lines, pulmonary ground-glass opacities indicating alveolar oedema and enlargement of the left ventricle) were recorded (Figure 2).

Laboratory markers

The electronic patient files of all patients from both groups were reviewed for the presence of laboratory findings including serum levels of BNP and/or proBNP dating from a time frame of ± 60 days from the date of the CT examination. If present, these laboratory values were recorded.

Statistical analysis

All statistics were performed using Microsoft Excel® (Microsoft, Redmond, WA) 2010 for Windows and MedCalc® statistical software v. 12.7.0 (MedCalc Software, Ostend, Belgium).

Figure 2. A 59-year-old female patient with cardiac decompensation. Axial lung window image shows dilated pulmonary veins, bronchial cuffing, extensive bilateral ground-glass opacities indicating initial alveolar oedema and bilateral pleural effusion.

Unpaired Student's *t*-test was used for comparisons of means between the two groups. Spearman's correlation coefficient (r_s) was used for all bivariate correlation analyses. Values of r_s from 0 to 0.29, from 0.30 to 0.69 and >0.70 were considered weak, moderate and strong correlations, respectively.⁴ Receiver operating characteristic (ROC) analysis was used to test the discriminatory power of CT density measurements for the presence or absence of cardiac biomarker elevations and to define a threshold with optimal sensitivity and specificity values.

For all statistical tests, a *p*-value of <0.05 was considered to indicate statistical significance and of <0.001 to indicate high statistical significance.

RESULTS

Population characteristics

The total study population included 232 subjects.

In the congestion group (90 patients with signs of congestion), the mean age was 70 years [standard deviation (SD), 14 years; range, 15–92 years]. 38 patients were male, and 52 were female. The control group included 142 subjects (66 males and 76 females) with a mean age of 58 years (SD, 17 years; range, 17–93 years). The difference in mean age of 12 years between the two subgroups was highly significant.

Serum levels of BNP were available in 36 patients in the congestion group (40%) and in 14 patients (9.8%) in the control group and of proBNP in 28 patients in the congestion group (31%) and in 17 patients in the control group (12%). Both biomarkers were available in 27 patients in the congestion group (30%) and in 12 patients in the control group (8.4%) (Table 1).

Comparison of lung perfused blood volume values between congestion and control groups

A comparison of mean PBV values between the two groups revealed no significant difference of the iodine-related pulmonary enhancement ($67 \pm 20\%$ in congestion group vs $71 \pm 18\%$ in control group) (Table 2).

Comparison of pulmonary arterial and left atrial enhancement and enhancement differences (PA – LA)

The mean enhancement values in the pulmonary trunk as well as in the left atrium differed significantly between the congestion and control groups with higher density values in the PA and

lower density in the LA in patients with signs of pulmonary congestion indicating a prolonged pulmonary passage of the contrast bolus. Furthermore, there was a highly significant difference ($p < 0.001$) of the mean values of the individual enhancement differences (PA – LA values) between the congestion and control groups (Table 2).

Comparison of CT-derived functional parameters of patients with and without cardiac peptide elevations Using a cut-off value of 100 pg ml^{-1} for BNP (as suggested in the description of the used assay ADVIA Centaur® Siemens Healthcare) and 125 pg ml^{-1} for proBNP (Elecsys® proBNP, Hoffmann-La Roche, Basel, Switzerland),^{5,6} we compared the differences of lung PBV and enhancement difference (PA – LA) in patients with and without elevated peptides indicating left heart failure, regardless of their initial allocation to the congestion or the control group. 38 patients had elevated BNP values (mean, 591 pg ml^{-1} ; SD, 634 pg ml^{-1}), whereas 13 did not (mean, 36 pg ml^{-1} ; SD, 24 pg ml^{-1}). We found significant differences for PBV, which was significantly lower with elevated BNP, as well as for the enhancement difference (PA – LA), which was higher with elevated BNP. A ProBNP elevation was found in 41 patients (mean, 2025 pg ml^{-1} ; SD, 2245 pg ml^{-1}), whereas 5 patients had serum values $<125 \text{ pg ml}^{-1}$ (mean, 62 pg ml^{-1} ; SD, 50 pg ml^{-1}). Here, a significant difference between the two groups was found in mean enhancement difference (PA – LA), whereas the difference in mean PBV did not reach statistical significance (Table 3).

A subanalysis of the patients with elevated cardiac markers from the initial Group #2 (control group) was then performed. In this group, 9 patients had BNP elevation (mean, 435 pg ml^{-1} ; SD, 561 pg ml^{-1}) and 14 patients had proBNP elevation (mean, 861 pg ml^{-1} ; SD, 970 pg ml^{-1}). Again, enhancement difference values were higher in the patients with biomarker elevations in comparison with all patients without biomarker elevations (for BNP: $111 \pm 101 \text{ HU}$ vs $39 \pm 72 \text{ HU}$; for proBNP: $100 \pm 123 \text{ HU}$ vs $17 \pm 24 \text{ HU}$). However, owing to the small number of patients in this subgroup, these differences were not statistically significant.

Receiver operating characteristic analysis

Patients with at least one cardiac biomarker exceeding the thresholds of 100 pg ml^{-1} for BNP and 125 pg ml^{-1} for proBNP were pooled ($n = 45$). The “negative group” (patients with at least one normal biomarker and no elevated alternative biomarker) contained 14 individuals. For enhancement difference (PA – LA), ROC analysis revealed a moderate discriminatory power for the

Table 1. Patient demographics

	Age, range (years)	Mean age (years)	% males	BNP available	proBNP available	BNP and proBNP available
Congestion group, $n = 90$	15–92	70 ^a	42	36	28	27
Control group, $n = 142$	17–93	58 ^a	46	14	17	12

BNP, B-type natriuretic peptide.

^aStatistically significant difference.

Table 2. Differences in lung perfused blood volume (PBV), pulmonary artery (PA) and left atrium (LA) enhancement and enhancement difference (PA – LA) between the two groups

	PBV (%)	PA enhancement (HU)	LA enhancement (HU)	EnhDiff (PA – LA) (HU)
Congestion group, <i>n</i> = 90	67 (20)	331 (115)	222 (74)	109 (103)
Control group, <i>n</i> = 142	71 (18)	294 (76)	250 (60)	51 (75)
<i>p</i> -value	NS	<0.05	<0.05	<0.001

EnhDiff, enhancement difference; NS, not significant.

The values in the table are represented as mean (standard deviation).

discrimination of patients with or without cardiac biomarker elevations (area under the ROC curve, 0.76). A cut-off value of 44 HU showed 76% sensitivity and 71% specificity (Figure 3).

Correlation analyses

Looking at the patients from both groups with documented BNP (*n* = 50) and/or proBNP (*n* = 45) values, we found a moderate correlation ($r_s = 0.40$) between enhancement difference (PA – LA) and serum BNP ($p < 0.05$). Furthermore, a moderate, highly significant correlation of enhancement difference (PA – LA) and proBNP levels ($r_s = 0.58$; $p < 0.001$) could be found (Figure 4). There was no significant correlation of lung PBV values and serum peptide levels.

DISCUSSION

Owing to a high overall morbidity with age-dependent increasing prevalence, left heart failure is a common condition in elderly patients,⁷ and radiologists have to keep in mind that typical findings of congestive heart failure can be found to a considerable degree in thoracic CT examinations as an incidental finding or an unsuspected cause of acute chest pain or dyspnoea.

With this study, using a retrospective approach, we aimed to investigate if there are significant discrepancies in pulmonary PBV values, as determined with DE-CTPA, in patients with signs of pulmonary congestion. Furthermore, we aimed to find out whether density measurements in the pulmonary trunk and the left atrium can be helpful in the assessment of haemodynamic changes caused by heart failure. We tested our hypotheses using a comparison of CT-derived absorption measurements, including DE-based PBV, in patients with suspected heart failure and patients without any cardiopulmonary pathology in CT. In addition, we correlated our measurements with the serum levels of cardiac biomarkers, where possible.

Our results could not support the hypothesis that signs of pulmonary congestion lead to a significantly increased X-ray pulmonary parenchymal beam absorption caused by an increased amount of contrast material in the lung volume on DE-CTPA. In contrast to this primary thesis, the impressive differences in PA and LA absorption values indicate that the pulmonary passage of the contrast bolus is markedly and measurably delayed in patients with left heart failure, regardless of a possibly increased actual pulmonary blood content. This reasoning is supported by our finding that elevated serum levels of BNP were significantly correlated with lower instead of higher PBV values. In addition, owing to the upper threshold settings of the DE PBV algorithm, which is designed to quantify lung parenchymal enhancement but not enhancement in the great vessels, an increased intravascular blood volume as a result of pulmonary venous dilatation would be missed even if the examination is adapted to a delayed pulmonary passage of the contrast bolus. The reason is that density values in the great pulmonary vessels normally exceed the upper threshold of the lung PBV algorithm.

However, there are previous studies that are helpful in the interpretation of our findings regarding lung PBV: in a recent study, Ugander et al⁸ investigated the changes in pulmonary blood volumes and their variations through the cardiac cycle in a pig model with induced myocardial infarction using MRI. Interestingly, they could not find a significant change in the pulmonary blood volume as a result of myocardial infarction. However, a decrease in its cyclical variation was found to be significant in myocardial infarction. To explain this phenomenon, they suggested an increased pulmonary vasoconstriction due to an increased pressure in the pulmonary vasculature with sympathetic activation, eventually leading to no significant changes in pulmonary blood volume. Cao et al,⁹ using MRI in a more recent study, found a decrease in

Table 3. Differences in perfused blood volume (PBV) and enhancement difference pulmonary artery (PA)–left atrium (LA) between populations with and without cardiac biomarker elevations [i.e. serum level of $>100 \text{ pg ml}^{-1}$ B-type natriuretic peptide (BNP) or $>125 \text{ ml}^{-1}$ proBNP]

	Elevated BNP (<i>n</i> = 38)	Normal BNP (<i>n</i> = 13)	<i>p</i> -value	Elevated proBNP (<i>n</i> = 41)	Normal proBNP (<i>n</i> = 5)	<i>p</i> -value
PBV (%)	64 (15)	83 (26)	<0.05	66 (19)	74 (16)	NS
EnhDiff (PA – LA) (HU)	129 (97)	39 (72)	<0.05	120 (110)	17 (24)	<0.05

EnhDiff, enhancement difference; NS, not significant.

The values in the table are represented as mean (standard deviation).

Figure 3. The receiver operating characteristic (ROC) curve demonstrates a moderate discriminatory power for patients with or without cardiac biomarker elevations (area under the ROC curve, 0.76). A cut-off value of 44HU showed 76% sensitivity and 71% specificity for serum elevation of at least one biomarker. EnhDiff, enhanced difference.

global pulmonary perfusion with decreasing cardiac index and underlined the complexity of cardiopulmonary interactions in determining pulmonary haemodynamics in left heart failure.

Density measurements in the PA and the LA and, especially, the intra-individual difference of these absorption values differed significantly in patients with congestive heart failure in contrast to non-congestion individuals. Thus, these easy-to-perform measurements that do not require a DE examination may be helpful in the diagnosis of left heart insufficiency, especially with regard to their objective character. Using this approach, functional haemodynamic impairment can be assessed alternatively or in addition to a rater-dependent evaluation on the basis of morphologic findings. Our assumption of a clinical significance

of these density measurements is supported by the correlation with BNP and with proBNP, cardiac biomarkers that strongly correlate with heart failure.^{10–14}

The finding of a delayed pulmonary passage of contrast material, indicating a prolonged pulmonary circulation time, which is reflected in increased PA density and reduced LA density, is in accordance with previous studies including a study of Shors *et al*¹⁵ from 2003. Using MR angiography, this group found significantly prolonged cardiopulmonary transit times in patients with heart failure and left ventricular dysfunction in comparison with a healthy control group. Furthermore, a correlation of the cardiopulmonary transit times with left ventricular end-diastolic and end-systolic volumes and an inverse correlation with the left ventricular ejection fraction were shown.

In our opinion, conspicuous PA and LA density measurements may suggest left heart failure but may not allow a grading of functional impairment, nor a discrimination of systolic or diastolic impairment. The actual clinical value of our findings, which to our knowledge have not been described before, seems to be an interesting subject for future prospective studies. A standardized examination with a fixed contrast injection protocol and delay is the pre-requisite for an effective implementation of this potential clinical tool and for the development of (site-specific) ranges of normal and pathological findings.

Our study has several limitations. We are using laboratory markers as a substitute for a clinical diagnosis of left heart failure with known ejection fractions and New York Heart Association (NYHA) functional classes. Even if cardiac biomarker elevations are known to be correlated with NYHA class and the severity of left ventricular systolic and diastolic dysfunction, there are clinical conditions (*i.e.* obesity, renal insufficiency and anaemia) that dramatically reduce their significance.^{13,16} Those confounding variables were not considered in our analysis. Also, in order to achieve a sufficient study population, we included laboratory values from dates up to 60 days from the CT examinations and did not differentiate between acute and chronic left heart failure. In addition, cardiac biomarkers were available only in a minority of our patients.

Figure 4. Visualization of a moderate, highly significant correlation of enhancement difference [pulmonary artery (PA) – left atrium (LA) enhancement values] and proB-type natriuretic peptide levels (Spearman's correlation coefficient $r_s = 0.58$; $p < 0.001$).

In order to keep a potential clinical tool “easy to handle”, we did not correct PBV values for patients’ age, as recently suggested by Meinel et al.¹ Our results might further have been influenced by this simplification.

In conclusion, using DE-CTPA, our study could not support our initial hypothesis of an increased PBV in patients with left heart failure due to pulmonary congestion. However, marked differences in HU measurements in the pre- and post-pulmonary

vessels between patients with and without heart failure are indicative of significantly altered haemodynamics. These measurements, which are not time consuming and do not require dual-energy CT (DECT), may be a helpful tool in patients with dyspnoea or chest pain when PE can be excluded.

FUNDING

This study was supported by the University of Munich.

REFERENCES

- Meinel FG, Graef A, Sommer WH, Thierfelder KM, Reiser MF, Johnson TR. Influence of vascular enhancement, age and gender on pulmonary perfused blood volume quantified by dual-energy-CTPA. *Eur J Radiol* 2013; **82**: 1565–70. doi: [10.1016/j.ejrad.2013.04.019](https://doi.org/10.1016/j.ejrad.2013.04.019)
- Schenzle JC, Sommer WH, Neumaier K, Michalski G, Lechel U, Nikolaou K, et al. Dual energy CT of the chest: how about the dose? *Invest Radiol* 2010; **45**: 347–53. doi: [10.1097/RLI.0b013e3181df901d](https://doi.org/10.1097/RLI.0b013e3181df901d)
- Meinel FG, Graef A, Bamberg F, Thieme SF, Schwarz F, Sommer WH, et al. Effectiveness of automated quantification of pulmonary perfused blood volume using dual-energy CTPA for the severity assessment of acute pulmonary embolism. *Invest Radiol* 2013; **48**: 563–9. doi: [10.1097/RLI.0b013e3182879482](https://doi.org/10.1097/RLI.0b013e3182879482)
- Gerstman BB. StatPrimer (Version 6.4). [cited 15 December 2013]. Available from: <http://www.sjsu.edu/faculty/gerstman/Stat-Primer/correlation.pdf>
- Al-Barjas M, Nair D, Ayrton P, Moris R, Davar J. How can the role of N terminal pro B natriuretic Peptide (NT-proBNP) be optimised in heart failure screening? A prospective observational comparative study. *Eur J Heart Fail* 2004; **3**: 51.
- Gustafsson F, Badskjær J, Stensgaard Hansen F, Poulsen AH, Hildebrandt P. Value of N-terminal proBNP in the diagnosis of left ventricular systolic dysfunction in primary care patients referred for echocardiography. *Heart Drug* 2003; **3**: 141–6.
- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Executive summary: heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation* 2013; **127**: 143–52.
- Ugander M, Kanski M, Engblom H, Gotberg M, Olivecrona GK, Erlinge D, et al. Pulmonary blood volume variation decreases after myocardial infarction in pigs: a quantitative and noninvasive MR imaging measure of heart failure. *Radiology* 2010; **256**: 415–23.
- Cao JJ, Wang Y, McLaughlin J, Rhee P, Passick M, Ngai N, et al. Effects of hemodynamics on global and regional lung perfusion: a quantitative lung perfusion study by magnetic resonance imaging. *Circ Cardiovasc Imaging* 2012; **5**: 693–9. doi: [10.1161/CIRCIMAGING.112.973206](https://doi.org/10.1161/CIRCIMAGING.112.973206)
- Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur J Heart Fail* 2008; **10**: 933–89.
- James SK, Lindahl B, Siegbahn A, Stridsberg M, Venge P, Armstrong P, et al. N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open occluded arteries (GUSTO)-IV substudy. *Circulation* 2003; **22**: 275–81.
- Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002; **18**: 161–7. doi: [10.1056/NEJMoa020233](https://doi.org/10.1056/NEJMoa020233)
- Palazzuoli A, Gallotta M, Quatrini I, Nuti R. Natriuretic peptides (BNP and NT-proBNP): measurement and relevance in heart failure. *Vasc Health Risk Manag* 2010; **6**: 411–18.
- Silver MA, Maisel A, Yancy CW, McCullough PA, Burnett JC Jr, Francis GS, et al. BNP Consensus Panel 2004: a clinical approach for the diagnostic, prognostic, screening, treatment monitoring, and therapeutic roles of natriuretic peptides in cardiovascular diseases. *Congest Heart Fail* 2004; **10**(5 Suppl. 3): 1–30.
- Shors SM, Cotts WG, Pavlovic-Surjancev B, Francois CJ, Gheorghiadu M, Finn JP. Heart failure: evaluation of cardiopulmonary transit times with time-resolved MR angiography. *Radiology* 2003; **229**: 743–8. doi: [10.1148/radiol.2293021363](https://doi.org/10.1148/radiol.2293021363)
- Nakane T, Kawai M, Komukai K, Kayama Y, Matsuo S, Nagoshi T, et al. Contribution of extracardiac factors to the inconsistency between plasma B-type natriuretic peptide levels and the severity of pulmonary congestion on chest X-rays in the diagnosis of heart failure. *Intern Med* 2012; **51**: 239–48.